### PATENT COOPERATION TREATY

	From the INTERNATIONAL BUREAU
PCT	To:
NOTIFICATION OF ELECTION  (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE
Date of mailing (day/month/year) 18 May 2000 (18.05.00)	in its capacity as elected Office
International application No. PCT/US98/08716	Applicant's or agent's file reference 00246/222WO1
International filing date (day/month/year) 30 April 1998 (30.04.98)	Priority date (day/month/year)
Applicant	
McMAHON, Andrew, P. et al	
in a notice effecting later election filed with the Inte	ry Examining Authority on: r 1999 (24.11.99)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Claudio Borton
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

### Copy for the Elected Office (EO/US)

### PATENT COOPERATION TREATY

	From the INTERNATIONAL BUREAU	J		
PCT	То:			
NOTIFICATION OF THE RECORDING OF A CHANGE  (PCT Rule 92bis.1 and Administrative Instructions, Section 422)  Date of mailing (day/month/year) 23 August 2000 (23.08.00)	BEATTIE, Ingrid, A. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC One Financial Center Boston, MA 02111 ETATS-UNIS D'AMERIQUE			
Applicant's or agent's file reference	MADORTANIT NOTIFICAT			
00246/222WO1	IMPORTANT NOTIFICAT	ION		
International application No. PCT/US98/08716	International filing date (day/month/year) 30 April 1998 (30.04.98)			
The following indications appeared on record concerning:				
the applicant the inventor	the agent the common repre	sentative		
Name and Address	State of Nationality State	of Residence		
FREEMAN, John, W. Fish & Richardson P.C.	Telephone No.			
225 Franklin Street Boston, MA 02110-2804	617-542-5070			
United States of America	Facsimile No. 617-542-8906			
	Teleprinter No.			
2. The International Bureau hereby notifies the applicant that t	e following change has been recorded concerni	ng:		
X the person X the name X the add	ess the nationality the	residence		
Name and Address	State of Nationality State	of Residence		
BEATTIE, Ingrid, A. Mintz, Levin, Cohn, Ferris,	Telephone No.			
Glovsky and Popeo PC One Financial Center	617-542-6000	<u> </u>		
Boston, MA 02111 United States of America	Facsimile No.	· · · ·		
	617-542-2241 Tele conter No.	<del></del>		
	Tele Anter No.			
3. Further observations, if necessary:				
4. A copy of this notification has been sent to:				
X the receiving Office	the designated Offices concern	ed		
the International Searching Authority	X the elected Offices concerned			
X the International Preliminary Examining Authority	other:			
The International Process (WIDO	Authorized officer			
The International Bureau of WIPO 34, chemin des Colombettes	I. Britel			
<b>1211 Geneva 20, Switzerland</b> Facsimile No.: (41-22) 740.14.35	Felephone No.: (41-22) 338.83.38			

### PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY JOHN W. FREEMAIN
FISH & RICHARDSON P.C.
225 FRANKLIN STREET
BOSTON, MASSACHUSETTS 02110-260 ECFVETHE

915198 SEP 03 1250 NOTIFICATION OF TRANSMITTAL OF HE INTERNATIONAL SEARCH REPORT OR THE DECLARATION Resp to scarchikept (PCT Rule 44.1) .nitials: **31 AUG** 1998 Applicant's or agent's file reference FOR FURTHER ACTION See paragraphs 1 and 4 below 00246/222WO1 International filing date International application No. (day/month/year) 04 MAY 1998 PCT/US98/08716 Applicant PRESIDENT AND FELLOWS OF HARVARD COLLEGE 1. X The applicant is hereby notified that the international search report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made. 4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II. Name and mailing address of the ISA/US Authorized officer

ROBERT C. HAYES, PH.D.

(703) 308-0196

Telephone No

Commissioner of Patents and Trademarks

Washington, D.C. 20231

Facsimile No. (703) 305-3230

### PATENT COOPERATION TREATY

### **PCT**

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 00246/222WO1	FOR FURTHER ACTION			ational Search Report plicable, item 5 below.
International application No.	International filing date	(day/month/year)	(Earliest) I	Priority Date
PCT/US98/08716	04 MAY 1998		NONE	
Applicant PRESIDENT AND FELLOWS OF HA	ARVARD COLLEGE			
This international search report has been according to Article 18. A copy is bein			hority and is transm	itted to the applicant
This international search report consist	s of a total of <u>5</u> sheets			
X It is also accompanied by a			eport.	
1. Certain claims were found	unsearchable (See Box 1	).		
2. X Unity of invention is lacking	ng (See Box II).			
3. The international application international search was carr			amino acid seque	ence listing and the
	filed with the international	application.		
<u> </u>	furnished by the applicant	separately from the	international applic	ation,
but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.				
	transcribed by this Author			
4. With regard to the title, X	the text is approved as su	bmitted by the applic	cant.	
	the text has been establish	ed by this Authority	to read as follows:	
5. With regard to the abstract,				
	the text is approved as su	bmitted by the appli	cant.	
X	the text has been establish in Box III. The applican international search report	t may, within one i	nonth from the dat	
6. The figure of the drawings to be p	published with the abstract	is:		
Figure No.	as suggested by the applic	cant.		None of the figures.
Ī	because the applicant faile	ed to suggest a figur	e	rione of the figures.
	because this figure better	characterizes the inv	ention.	

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
-
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-13
Remark on Protest  The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

International application No. PCT/US98/08716

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The old Abstract included a Title, which is now deleted.

### **NEW ABSTRACT**

An enriched population of mammalian dorsal neural progenitor cells, e.g., dopaminergic neural precursor cells, are described that are useful to induce neuronal regeneration in mammals suffering from a neurodegenerative disease.



A. CLASSIFICATION OF SUBJECT MATTER  IPC(6) :C12N 5/06, 5/08						
US CL :435/325, 368, 377 According to International Patent Classification (IPC) or to both national classification and IPC						
<u> </u>						
	ocumentation searched (classification system followed	by classification symbols)				
U.S. :	435/325, 368, 377					
Documentat	ion searched other than minimum documentation to the	extent that such documents are included	in the fields searched			
Electronic d	ata base consulted during the international search (na	me of data base and, where practicable	, search terms used)			
	SIS, MEDLINE ms: neural, precursor#, progenitor, stem, cell#, human	, porcine, wnt#, dorsal, hippocam##, hi	ndbrain, dopamin?			
C. DOC	UMENTS CONSIDERED TO BE RELEVANT					
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.			
X	US 5,411,883 A (BOSS et al) 02 May	1995, columns 3, 7, 11-13,	1-9 			
Y	17 and 19-20.		10-13			
x	X US 5,589,376 A (ANDERSON et al) 31 December 1996, columns					
  A	3-4, 8-9, 11, 13-14 and 16-17.					
X .						
X	US 5,656,481 A (BAETGE et al) 12 A 46-57.	ugust 1997, column 30, lines	1, 11-13			
Furt	Further documents are listed in the continuation of Box C. See patent family annex.					
*A* do	Special categories of cited documents:  "A" document defining the general state of the art which is not considered to be of particular relevance  "A" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention					
.L. do	*L* document which may throw doubts on priority claim(s) or which is when the document is taken alone					
*O* do	cited to establish the publication date of another citation or other special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other combined with one or more other such documents, such combination					
•P• do	· · · · · · · · · · · · · · · · · · ·					
	actual completion of the international search	Date of mailing of the international se	arch report			
Commissi Box PCT	Washington, D.C. 20231					

International application No. PCT/US98/08716

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-13, drawn to a population of mammalian neural precursor cells committed to a cell fate.

Group II, claim(s) 14-16, drawn to a method of stimulating proliferation of a heterogenous population of neural cell precursor cells to enrich for dorsal neural cells.

Group III, claim(s) 17-18 and 20, drawn to a method of inducing neuronal regeneration in an adult mammal comprising transplanting dorsal neural precursor cells.

Group IV, claim(s) 19, drawn to a method of inducing neuronal regeneration in an adult mammal comprising administering a Wnt polypeptide or Wnt agonist.

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I is directed to a population of mammalian neural precursor cells, which is the first product. However, because Boss et al teach an enriched population of porcine or human neuron progenitor cells (i.e., mammalian neural precursor cells), no special technical feature exists for Group I as defined by PCT RULE 13.2, because it does not define a contribution over the prior art. The technical features of Groups II-IV are drawn to methods having different goals, method steps and starting materials, which do not share the same or a corresponding technical feature. Note that PCT Rule 13 does not provide for multiple products or methods within a single application. Because the technical feature of Group I is not a special technical feature, and because the technical features of the Group II-IV inventions are not present in the Group I claims, unity of invention is lacking.

# CHAPTER I PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

● 09/674292 526 Rec'd PCT/FTD 300CT 2000



PCT No.: PCT/US98/08716

Examiner: ROBERT C. HAYES, PH.D.

Attorney spoken to: JOHN FREEMAN

Date of call: 23 JULY 1998

☐ Amount of payment approved:	
☐ Deposit account number to be charged:	
☐ Attorney elected to pay for <u>ALL</u> additional inventions	
☐ Attorney elected to pay only for the additional inventions covered by	
$\square$ Group(s):	
encompassing	
☐ Claim(s):	
Attorney elected <b>NOT</b> to pay for any additional inventions, therefore, only claimed invention (Group I) covered by Claim(s) 1-13 has been searched.	the first

### Attorney was orally advised that there is no right to protest for any group not paid for.

Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

### Time Limit For Filing A Protest

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

### Detailed Reasons For Holding Lack Of Unity Of Invention:

### Detailed Reasons For Holding Lack of Unity Of Invention:

(Continued on a separate sheet)

Note: A copy of this form must be attached to the Search Report.

## ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

#### Detailed Reasons For Holding Lack Of Unity Of Invention:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-13, drawn to a population of mammalian neural precursor cells committed to a cell fate.

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### **PCT**

### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



51) International Patent Classification <sup>6</sup> : C12N 5/06, 5/08	A1		1) International Publication Number: WO 99/57248
		(4	3) International Publication Date: 11 November 1999 (11.11.99
21) International Application Number: PCT/U 22) International Filing Date: 30 April 1998	JS98/087 (30.04.9		(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
71) Applicant (for all designated States except US): PR AND FELLOWS OF HARVARD COLLEGE [U Quincy Street, Cambridge, MA 02138 (US).			Published With international search report.
72) Inventors; and 75) Inventors/Applicants (for US only): McMAHON, A [GB/US]; 128 Kendall Road, Lexington, MA 02 LEE, Scott, K. [US/US]; 54 Chestnut Street, O MA 02139 (US). TAKADA, Shinji [-/-]; -	2173 (US	S).	
74) Agent: FREEMAN, John, W.; Fish & Richardson Franklin Street, Boston, MA 02110-2804 (US).	P.C., 2	25	
54) Title: INDUCTION OF NEURONAL REGENERA	ATION		
57) Abstract			
An enriched population of mammalian dorsal neural seful to induce neuronal regeneration in mammals suffe			cells, e.g., dopaminergic neural precursor cells, are described that ar neurodegenerative disease.

### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	1.1	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

Form PCT/ISA/210 (second sheet) July 1992) \*

A. CLASSIFICATION OF SUBJECT MATTER  IPC(6) :C12N 5/06, 5/08  US CL :435/325, 368, 377  According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIEI	LDS SEARCHED			
Minimum o	documentation searched (classification system follow 435/325, 368, 377	ed by classification symbols)		
Documenta	tion searched other than minimum documentation to th	ne extent that such documents are included	in the fields searched	
Electronic	data base consulted during the international search (n	name of data base and, where practicable	, search terms used)	
APS, BIC	DSIS, MEDLINE rms: neural, precursor#, progenitor, stem, cell#, huma			
C. DOC	CUMENTS CONSIDERED TO BE RELEVANT			
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.	
X	US 5,411,883 A (BOSS et al) 02 Ma	y 1995, columns 3, 7, 11-13,	1-9	
Y	17 and 19-20.		10-13	
X	US 5,589,376 A (ANDERSON et al)	31 December 1996, columns	1	
A	- 3-4, 8-9, 11, 13-14 and 16-17.			
MOYER et al. Culture, Expansion, and Transplantation of Human Fetal Neural Progenitor Cells. Transplantation Proceedings. June 1997, Vol. 29, No. 4, pages 2040-2041, see entire document.				
X	X US 5,656,481 A (BAETGE et al) 12 August 1997, column 30, lines 1, 11-13 46-57.			
Further documents are listed in the continuation of Box C. See patent family annex.				
* Special categories of cited documents  *A* document defining the general state of the art which is not considered document defining the general state of the art which is not considered the principle or theory underlying the invention.  *A* document defining the general state of the art which is not considered the principle or theory underlying the invention.				
to be of particular relevance  "E" carber document published on or after the international filing date  "L" document which may throw doubts on priority claim(s) or which is  "L" document which may throw doubts on priority claim(s) or which is				
cited to establish the publication date of another citation or other special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other means  *O* document referring to an oral disclosure, use, exhibition or other means				
*P* document published prior to the international filing date but later than "g." document member of the same patent family the priority date claimed				
Date of the actual completion of the international search  Date of mailing of the international search report				
30 ЛЛLY 1998 <b>31 AUG 1998</b>				
Commission Box PCT	nailing address of the ISA/US ner of Patents and Trademarks	Authorized officer  ROBERT C. HAYES, PH.D.	Jab	
Washington, D.C. 20231  Facsimile No. (703) 305-3230  Telephone No. (703) 308-			V 10	

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-13
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

International application No. PCT/US98/08716

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

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